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EXAMINER
SKELDING, ZACHARY S

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/642,642	ZIPORI ET. AL.	
	Examiner	Art Unit	
	Zachary Skelding	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *4,8-12,16 and 18-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7, 13-15 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-21-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election filed October 11, 2007, with traverse, is acknowledged.

Claims 1-26 are pending.

2. Applicant's election of the invention of Group I, drawn to polynucleotides comprising a transcript of a T cell receptor gene, said polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequence upstream to said J region sequence including an in frame methionine codon, wherein the species of C domain, J region and 5' intronic J sequences are "Jβ", and the particular species of intronic Jβ sequence is the intronic Jβ sequence upstream of Jβ2.6 which encodes SEQ ID NO: 2, with traverse, in the reply filed October 11, 2007 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)), and the restriction requirement has been made FINAL.

Upon further consideration, the species of Jβ intronic sequence to be examined has been extended to include the intronic Jβ sequence upstream of Jβ2.3 which encodes SEQ ID NO: 17.

Thus, claims 1-3, 5-7, 13-15 and 17 are under examination as they read on polynucleotides comprising a transcript of a T cell receptor gene, said polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequence upstream to said J region sequence including an in frame methionine codon, wherein the species of C domain, J region and 5' intronic J sequences are "Jβ", and the particular species of intronic Jβ sequences are the intronic Jβ sequences upstream of Jβ2.3 and Jβ2.6 which encode the polypeptides of SEQ ID NOs: 17 and 2, respectively.

Furthermore, claims 4, 8-12, 16 and 18-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species of invention, there being no allowable generic or linking claim.

3. It is noted that due to the death of Inventor Rozenszajn on February 18, 2003, the oath or declaration filed March 15, 2004 has been signed on his/her behalf by legal representative of the assignee of the full interest of Inventor Rozenszajn, Bar-Ilan University.

4. Claim 6 is objected to because there should be a space between "5'" and "intronic" consistent with the nomenclature in the other claims and throughout the specification, see for example claim 1 and the instant specification at page 4, 4th paragraph.

5. The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claim 17 is rejected under 35 USC § 101 because the claimed invention is directed to non-statutory subject matter, a product of nature.

The instant claim recites "a polynucleotide comprising SEQ ID NO: 38". However the instant claims, as written, do not sufficiently distinguish over naturally occurring polynucleotides, for example naturally occurring polynucleotides comprising SEQ ID NO: 38 as they occur in the mouse, because the claims do not particularly point out any non-naturally occurring differences between the claimed polynucleotides and naturally occurring polynucleotides. In the absence of the hand of man, naturally occurring polynucleotides are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980).

Applicant should amend the instant claim to indicate the hand of man and point to a basis in the specification so as not to add new matter. See MPEP 2163.06.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-3, 5-7 and 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "[a]n isolated polynucleotide comprising a transcript of a T cell receptor (TCR) gene, said polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream to said J region sequence including an in-frame methionine codon."

However, the metes and bounds of claim 1, and dependent claims thereof, are unclear.

In particular, it is unclear if what is being claimed is an isolated polynucleotide which comprises "a transcript of a T cell receptor (TCR) gene" as well as "a constant (C) domain and joining (J) region…" or if what is being claimed is an isolated polynucleotide which comprises "a transcript of a T cell receptor (TCR) gene" and that the transcript itself further comprises "a constant (C) domain and joining (J) region….".

Moreover, it is additionally unclear what is meant by the phrase "including an in-frame methionine codon" in claim 1. In particular, it is unclear what the reference point is for the "in-frame methionine codon," i.e., what is the reference polypeptide that the methionine codon is "in-frame" with?

Also, claim 15 recites "[t]ransfected mesenchymal human cells according to claim 14," wherein claim 14 is drawn to "[a] host cell comprising a vector…wherein the host is a mammalian cell."

However, the metes and bounds of claim 1 and dependent claims thereof are unclear. In particular, it is unclear if claim 15 refers to the host cell of claim 14 which already comprises a vector transfected with something else or if it refers to the host cell of claim 14 not additionally transfected with something else but rather further limited in that said mammalian cell of claim 14 is a mesenchymal cell.

Thus, the instant claims fail to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-3, 5-7 and 13-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated polynucleotides encoding the polypeptides of SEQ ID NOs: 37, 39 or 2, such as SEQ ID NO: 38 which encodes SEQ ID NO: 39, does not reasonably provide enablement for any isolated polynucleotide wherein said isolated polynucleotide comprises a transcript of a T cell receptor (TCR) gene, the polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The disclosure of the specification does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states on page 1404, "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The instant claims, given their broadest reasonable interpretation consistent with the instant specification, read on any isolated polynucleotide comprising a transcript of a T cell receptor (TCR) gene, the polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon (see instant specification, pages 4-7).

The knowledge in the art pertaining to using any isolated polynucleotide comprising a transcript of a T cell receptor (TCR) gene, the polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequence, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon is low.

The instant specification asserts that the claimed polynucleotides encode polypeptides that have a variety of uses, such as for the modulation of mesenchymal cell growth or for making antibodies that can in turn be used for the detection of mesenchymal cells that can be used in would healing, for example, mouse embryonic fibroblasts, which are known by the skilled artisan to be pluripotent progenitor cells (see instant specification, in particular, page 3, 1st paragraph; the paragraph bridging pages 10-11 and page 33).

The instant specification further exemplifies a particular antibody raised against a polypeptide encoded by a segment of the 5' intronic sequence with an in-frame methionine codon upstream of Jβ2.6, i.e., SEQ ID NO: 37 (note that SEQ ID NO: 37 is contained within SEQ ID NO: 2 which is contained within SEQ ID NO: 39). The instant specification shows that said antibody is useful for the detection of mouse embryonic fibroblasts, which are known by the skilled artisan to be pluripotent progenitor cells that are useful in wound healing (see, in particular, page 3, 1st paragraph; page 11, description of Figs. 2A-2F and pages 27-28, Examples 1 and 2).

The instant specification further discloses that "a molecule such as Jint-Jβ2.1-Cβ2" can be detected in the tumorogenic mesenchymal cell line MBA-13 "using appropriate primers" (see, in particular, page 28, 3rd paragraph).

The instant specification also discloses that a polynucleotide transcript of a T cell receptor (TCR) gene, the polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, wherein the joining J gene sequence is Jβ2.3, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon, wherein the 5' intronic sequence encodes SEQ ID NO: 17, was isolated from human cord blood mononuclear cells and human amniotic fluid cells (see instant specification at page 31, 3rd paragraph and SEQ ID NO: 67). The instant specification also discloses at page 32, 1st paragraph, that a fusion of the Jβ2.3 polynucleotide to GFP can be used to express a GFP-fusion protein (see instant specification at page 32, 1st paragraph).

However, neither the disclosure of the instant specification, nor the knowledge in the art are sufficient for the skilled artisan to make and use the claimed invention to its full breadth.

While antibodies raised against a polypeptide encoded by a segment of the 5' intronic sequence with an in-frame methionine codon upstream of Jβ2.6, i.e., SEQ ID NO: 37, are useful for detecting mouse embryonic fibroblasts which are useful, for example, in wound healing, the instant specification does not teach the skilled artisan how to make and use any isolated polynucleotide commensurate in scope with the claimed invention with any measure of predictability.

For example, while the instant specification discloses that PCR analysis detected the Jint-Jβ2.1-Cβ2 mRNA in the tumorogenic mesenchymal cell line MBA-13 as described above, a post-filing date publication contradicts the disclosure of the instant specification in that it shows mRNA analysis of the mesenchymal cell line MBA-13 does not detect Jint-Jβ2.1-Cβ2 (see Barda-Saad et al., Oncogene. 2002 Mar 27;21(13):2029-36, in particular, page 2032 Figure 2E, cited on IDS of January 21, 2005).

Thus, the skilled artisan would not know how to use Jint-Jβ2.1-Cβ2, without undertaking undue experimentation, to modulate mesenchymal cell growth or as a "diagnostic marker" for the detection of a mesenchymal cells that can be used in would healing for example, such as mouse embryonic fibroblasts.

Moreover, simply showing that a polynucleotide transcript of a T cell receptor (TCR) gene encompassed by the instant claims can be isolated from human cord blood mononuclear cells and human amniotic fluid cells, as is the case with SEQ ID NO: 67, does not provide sufficient direction or guidance for the skilled artisan to use SEQ ID NO: 67 as taught in the instant specification.

For example, before using SEQ ID NO: 67 or the polypeptide encoded thereby to modulate mesenchymal cell growth or to detect of mesenchymal cells that can be used in would healing, for example, mouse embryonic fibroblasts, the skilled artisan would first have to determine, at a minimum, which, if any mesenchymal cells express SEQ ID NO: 67.

However, this is not a matter of routine experimentation. "Mesenchymal cells" are a phenotypically heterogeneous population of cells including, for example, cells with pluripotentcy such as mesenchymal stem cells and fibroblast-like mesenchymal cells, as well as more highly differentiated cells such as endothelial-like mesenchymal cells, adipocytic mesenchymal cells, osteoblastic mesenchymal cells (see, for example, Benayahu et al., Calcif Tissue Int. 1991 Sep;49(3):202-7, in particular page 202). Moreover, these different types of mesenchymal cells have phenotypically diverse expression of many different markers such as alkaline phosphatase (see, Benayahu et al., ibid, in particular page 204, right column, 3rd paragraph) and extracellular matrix protein (see, Ziproi et al., Blood. 1985 Aug;66(2):447-55, in particular page 449, Table 1).

Given the variety of mesenchymal cells and their functional differences, the skilled artisan would not be able to reliably predict, which, if any polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon, other than SEQ ID NO: 38, would be useful for either modulating mesenchymal cell growth or detecting mesenchymal cells that can be used in would healing, and undue experimentation would be required to determine which particular transcripts, if any, are useful in this regard.

Similarly, given a particular species of polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon, i.e., SEQ ID NO: 38, is useful for the detection of mesenchymal cells that can be used in would healing, for example, mouse embryonic fibroblasts, which are known by the skilled artisan to be pluripotent progenitor cells, the skilled artisan would not be able to reliably predict that similar polynucleotides expressed in other animals, such as SEQ ID NO: 67 which the instant specification discloses can be isolated from human cord blood mononuclear cells and human amniotic fluid cells, is similarly useful for detecting human mesenchymal cells that can be used in would healing, such as human embryonic fibroblasts.

This is because not only is there very little known in the art about the expression and biological function of transcripts of a T cell receptor (TCR) gene, the polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon, but also the skilled artisan recognizes that gene expression is controlled by complex combinatorial regulatory sequences which diverge across species, e.g., mouse vs. human, and that differences in gene regulation underlie interspecies evolution. (see, for example, Carroll et al., Cell. 2000 Jun 9;101(6):577-80, in particular, page 577 and the section entitled "the evolution of regulatory DNA..." bridging pages 578-579).

In light of the inter-species variability in gene expression the skilled artisan would not be able to predict, with any degree of certainty and in the absence of objective evidence, if any given isolated naturally occurring species of polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon, such as SEQ ID NO: 67, would be useful for modulating mesenchymal cell growth or detecting mesenchymal cells that can be used in would healing, for example, human embryonic fibroblasts.

It is additionally noted that the instant specification further discloses appx. 30 other polynucleotides comprising a transcript of a T cell receptor (TCR) gene, the polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon (see instant specification pages 4-8).

However, the sequences of these polynucleotides were derived from database hunting and the instant specification does not appear to disclose if any of these polynucleotides have been detected as expressed transcripts in natural sources or provide any other objective evidence that these polynucleotides or the polypeptides they encode have useful properties.

For example, consider the "hypothetical" JαTA46 polypeptide and the polynucleotide that encodes said sequence (see instant specification at page 4(ii)-(iii)).

According to the instant specification, the claimed isolated polynucleotide can comprise the intronic sequences MAWH (SEQ ID NO: 3) or MEAGWEVQHWVSDMECLTV (SEQ ID NO: 4).

However, based on the teachings of the instant specification and the low level of knowledge in the art pertaining to the claimed subject matter, the skilled artisan would not know with any degree of predictability, which, if any isolated polynucleotide comprising a transcript of a T cell receptor (TCR) gene, the polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream of the J region sequence including an in-frame methionine codon, such as SEQ ID NOs: 3 or 4, would be useful for the modulation of mesenchymal cell growth or as a "diagnostic marker" for the detection of a mesenchymal cells that can be used in would healing.

In conclusion, the instant claims encompass an invention of tremendous breadth, and essentially call for trial and error by the skilled artisan to begin discovering how to use the claimed invention without assisting the skilled artisan in such an endeavor, which is insufficient to constitute adequate enablement.

The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Undue experimentation would be required to produce the invention commensurate with the breadth of the claims based on the disclosure of the instant specification and the knowledge in the art. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

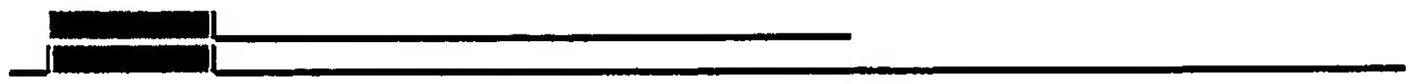
11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1, 2, 6, 7, 13 and 14 are rejected under 35 U.S.C. 102(e) as anticipated by Olga Bandman (US 20020137081) as evidenced by Entrez Nucleotide accession number L34740 (http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=nuccore&id=1100190), Entrez Protein accession number AAA82687 (http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?db=protein&id=1100191), and IGc domain description (http://www.ncbi.nlm.nih.gov/Structure/cdd/cddsrv.cgi?uid=28981).

Bandman teaches a human cDNA of 1186 nucleotides (SEQ ID NO:130) which is greater than 2.5 fold underexpressed in TNFα and/or IL-1 activated vascular smooth muscle cells relative to non-activated vascular smooth muscle cells, and thus can be used to diagnose or monitor the progression or treatment of atherosclerosis (See, in particular, pages 1-2, paragraphs [0002]-[0010] and page 3, paragraph [0022]). Bandman further teaches expression of the cDNAs of the invention by cloning into an expression vector and transfection of a mammalian host cells with said cDNA containing expression vector (see, in particular, pages 7-8, paragraphs [0081]-[0085]).

Nucleotides 35-173 of Bandman SEQ ID NO: 130 are identical to nucleotides 1-139 of SEQ ID NO: 67 of the instant specification as shown below where SEQ ID NO: 67 is the Query and Bandman SEQ ID NO: 130 is the Sbjct (alignment prepared using the BLAST two sequences program publicly available at http://www.ncbi.nlm.nih.gov/blast/bl2seq/ wblast2.cgi):



```
 Score =  267 bits (139),  Expect = 3e-68
 Identities = 139/139 (100%), Gaps = 0/139 (0%)
 Strand=Plus/Plus

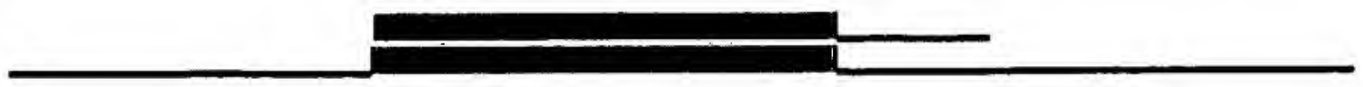
Query  1    ATGGGGCTCTCAGCGGTGGGAAGGACCCGAGCTGAGTCTGGGACAGCAGAGCGGGCAGCA  60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  35   ATGGGGCTCTCAGCGGTGGGAAGGACCCGAGCTGAGTCTGGGACAGCAGAGCGGGCAGCA  94

Query  61   CCGGTTTTTGTCCTGGGCCTCCAGGCTGTGAGCACAGATACGCAGTATTTTGGCCCAGGC  120
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  95   CCGGTTTTTGTCCTGGGCCTCCAGGCTGTGAGCACAGATACGCAGTATTTTGGCCCAGGC  154

Query  121  ACCCGGCTGACAGTGCTCG  139
            ||||||||||||||||||
Sbjct  155  ACCCGGCTGACAGTGCTCG  173
```

Given that nucleotides 1-139 of SEQ ID NO: 67 encode the polypeptide of SEQ ID NO: 17 (which starts with a methionine and is encoded by the intron 5' to Jβ2.3) fused to a Jβ2.3 polypeptide (see Amended Figure 11 filed May 3, 2006 in connection with the instant specification) nucleotides 35-173 of Bandman SEQ ID NO: 130 meet these limitations of the instant claims.

Furthermore, SEQ ID NO: 130 of Bandman further comprises nucleotides 325-730 which are identical but for 2 mismatches to nucleotides 1-406 of the polynucleotide sequence of the human TCR β chain constant (C) domain shown, for example, in Entrez Nucleotide accession number L34740, where SEQ ID NO: 130 of Bandman is the Sbjct and Entrez Nucleotide accession number L34740 is the Query (alignment prepared using the BLAST two sequences program publicly available at http://www.ncbi.nlm.nih.gov/blast/bl2seq/wblast2.cgi):



```
 Score =  769 bits (400),  Expect = 0.0
 Identities = 404/406 (99%), Gaps = 0/406 (0%)
 Strand=Plus/Plus

Query  1    GAGGACCTGAAAAACGTGTTCCCACCCGAGGTCGCTGTGTTTGAGCCATCAGAAGCAGAG  60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  325  GAGGACCTGAAAAACGTGTTCCCACCCGAGGTCGCTGTGTTTGAGCCATCAGAAGCAGAG  384

Query  61   ATCTCCCACACCCAAAAGGCCACACTGGTATGCCTGGCCACAGGCTTCTACCCCGACCAC  120
            |||||||||||||||||||||||| ||||||||||||||||||||||||||||||||||||
Sbjct  385  ATCTCCCACACCCAAAAGGCCACACTGGTGTGCCTGGCCACAGGCTTCTACCCCGACCAC  444

Query  121  GTGGAGCTGAGCTGGTGGGTGAATGGGAAGGAGGTGCACAGTGGGGTCAGCACAGACCCG  180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  445  GTGGAGCTGAGCTGGTGGGTGAATGGGAAGGAGGTGCACAGTGGGGTCAGCACAGACCCG  504

Query  181  CAGCCCCTCAAGGAGCAGCCCGCCCTCAATGACTCCAGATACTGCCTGAGCAGCCGCCTG  240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  505  CAGCCCCTCAAGGAGCAGCCCGCCCTCAATGACTCCAGATACTGCCTGAGCAGCCGCCTG  564

Query  241  AGGGTCTCGGCCACCTTCTGGCAGAACCCCCGCAACCACTTCCGCTGTCAAGTCCAGTTC  300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  565  AGGGTCTCGGCCACCTTCTGGCAGAACCCCCGCAACCACTTCCGCTGTCAAGTCCAGTTC  624

Query  301  TACGGGCTCTCGGAGAATGACGAGTGGACCCAGGATAGGGCCAAACCCGTCACCCAGATC  360
            |||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||
Sbjct  625  TACGGGCTCTCGGAGAATGACGAGTGGACCCAGGATAGGGCCAAACCTGTCACCCAGATC  684

Query  361  GTCAGCGCCGAGGCCTGGGGTAGAGCAGACTGTGGCTTCACCTCCG  406
            |||||||||||||||||||||||||||||||||||||||||||||
Sbjct  685  GTCAGCGCCGAGGCCTGGGGTAGAGCAGACTGTGGCTTCACCTCCG  730
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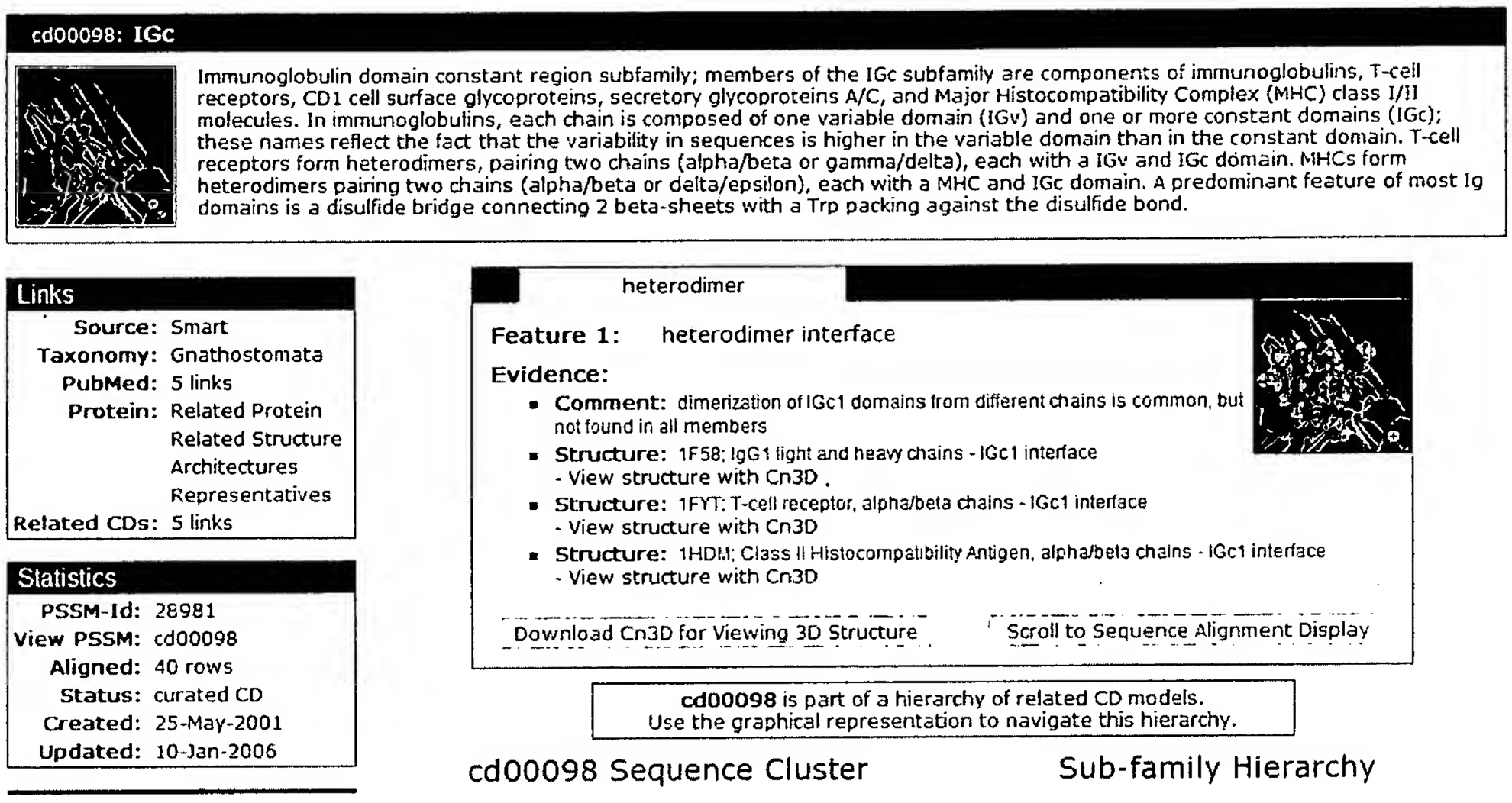
Furthermore, residues 325-730 of Bandman SEQ ID NO: 130 encode a polypeptide identical to the human TCR β chain constant (C) domain, in particular residues 1-135 of a human TCR β chain constant (C) domain shown, for example, in Entrez Protein accession number AAA82687 (note that the polypeptide of AAA82687 is encoded by Entrez Nucleotide accession number L34740 cited above).

As can be seen from the Entrez Protein accession number AAA82687, residues 6 to 108 AAA82687 correspond to the "IGc domain" of the human TCR β chain constant (C) domain which forms the heterodimer interface between the TCR β and α subunits:



(See http://www.ncbi.nlm.nih.gov/Structure/cdd/cddsrv.cgi?uid=28981 for additional information about the "IGc domain").

Thus, SEQ ID NO: 130 of Bandman encodes a TCR β constant domain.

Lastly, it noted that when considered as a whole, Bandman SEQ ID NO: 130 can be given the following nucleotide assignments:

Residues 1-124 – genomic region 5' of the human Jβ2.3 exon
Residues 125-324 - Jβ2.3 exon-intron-Jβ2.4 exon
Residues 325-1642 – exon 1- exon 2 – Cβ2 intron B – exon 3 – exon 4 of the 4 exon Cβ2 domain

Residues 1643-1186 – genomic region 3' of exon 4 of the Cβ2 domain

Thus, SEQ ID NO: 130 of Bandman is indeed a transcript of a TCR gene (which has 3 completed exon to exon junctions) and not a cloning artifact.

In conclusion, SEQ ID NO: 130 of Bandman anticipates the instant claims in that it is an isolated polynucleotide comprising a transcript of a T cell receptor (TCR) gene, said polynucleotide lacking V region sequences and comprising a constant (C) domain and joining (J) region sequences, and a 5' intronic J sequences upstream to said J region sequence including an in-frame methionine codon, wherein the intronic Jβ sequence is the intronic sequence upstream of Jβ2.3 which encodes the polypeptide of SEQ ID NO: 17. Moreover, Bandman teaches expression of the cDNAs of the invention by cloning into an expression vector and transfection of a mammalian host cells with said cDNA containing expression vector.

It should be noted that as stated in Rasmusson v. SmithKline Beecham Corp., *ibid*, "In In re Hafner, 410 F.2d 1403 (CCPA 1969), the court stated that 'a disclosure lacking a teaching of how to use a fully disclosed compound for a specific, substantial utility or of how to use for such purpose a compound produced by a fully disclosed process is, under the present state of the law, entirely adequate to anticipate a claim to either the product or the process and, at the same time, entirely inadequate to support the allowance of such a claim.' Id. at 1405; see Schoenwald, 964 F.2d at 1124; In re Samour, 571 F.2d 559, 563-64 (CCPA 1978). The reason is that **section 112 'provides that the specification must enable one skilled in the art to 'use' the invention whereas [section] 102 makes no such requirement as to an anticipatory disclosure.'** Hafner, 410 F.2d at 1405; see 1 Donald S. Chisum, Chisum on Patents § 3.04[1][c] (2002); see also In re Cruciferous Sprout Litig., 301 F.3d 1343, 1349-52 (Fed. Cir. 2001) (finding anticipation where applicant sought a patent based on a new use for a previously disclosed method)." (emphasis added).

More particularly, in Rasmusson v. SmithKline Beecham Corp (413 F.3d 1318, 1325-26 (Fed. Cir. 2005)), the Court of Appeals for the Federal Circuit held that prior art European patent application, EP No. 285383 ("EP '383") was **an enabled reference for purposes of anticipation** ***even though***, according to the United States Patent and Trademark Office, Board of Patent Appeals and Interferences, **(1)** there was no reasonable scientific basis for a person of ordinary skill in the art to conclude that the claimed method would be effective in treating prostate cancer, and **(2)** EP '383 did not provide any proof that the claimed method would actually be effective in treating prostate cancer.

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary Skelding whose telephone number is 571-272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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December 6, 2007

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PRIMARY EXAMINER
12/26/07